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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/420,433	10/12/1999	DAVID SIDRANSKY	JHU1180-1	2810

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EXAMINER	
JOHANNSEN, DIANA B	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 11/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/420,433	SIDRANSKY, DAVID	
	Examiner	Art Unit	
	Diana B. Johannsen	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 July 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,7-14,18-22 and 24-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,7-14,18-22 and 24-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

FINAL ACTION

1. This action is in response to the Amendment and Response filed July 23, 2004. Claims 7-8 have been amended, and claims 1-4, 7-14, 18-22 and 24-26 are now pending and under consideration. The amendments and arguments have been thoroughly reviewed, but are not persuasive for the reasons that follow. Any rejections not reiterated in this action have been withdrawn. **This action is FINAL.**

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112, first paragraph

3. Claims 1-4, 7-14, 18-22, and 24-26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement, for the reasons set forth in the Office action of March 24, 2004.

The response traverses the rejection on the following grounds. First, the response notes that the Deguchi et al reference cited by the examiner does not disclose p53 mutations but rather teaches detection of PSA in lymph node cells that appear histologically normal. The response goes on to argue that while PSA "can be distinguished from the claimed subject matter" in that it is "not a mutant nucleic acid," the Deguchi et al reference "provides objective evidence that...the presence of cancer cells other than head and neck cancer cells can be detected in tissue that appears to be histologically normal." Additionally, the response urges that, given the evidence provided in the specification regarding p53 mutations, one of skill in the art "would have known that the claimed methods could be practiced with respect to" the mutant nucleic

acids of the claims, as Applicant's disclosures regarding p53 provide "the general teaching that tumor cells that metastasize from a primary tumor can be identified in otherwise normal appearing tissues."

These arguments have been thoroughly considered but are not persuasive for the following reasons. First, it is acknowledged that the rejection set forth in the prior Office action incorrectly stated that the Deguchi et al reference discloses detection of p53 mutations in histologically normal lymph nodes, whereas the reference in fact teaches detection of PSA in such lymph nodes. However, it is noted that the Deguchi et al reference (in combination with the Nees et al reference) was merely cited by the examiner as supporting enablement of an (unclaimed, p53-related) invention that was already acknowledged by the examiner as being enabled by Applicant's own disclosure. Neither the Deguchi et al reference nor the Nees et al reference was relied upon as providing a greater scope of enablement than Applicant's disclosure, for example, by teaching early detection of any of the particular nucleic acids that are encompassed by Applicant's claims. While Applicant goes on to argue that the Deguchi et al reference provides evidence of another molecule (PSA) whose early detection in histologically normal cells can be detected as in indicator of cancer, PSA is not a "mutant nucleic acid" within the context of the claimed invention (as Applicant has acknowledged), and detection of PSA is not in fact encompassed by the instant claims. Thus, the early detection of PSA reported by Deguchi et al does not support enablement of the claimed invention. As discussed in the prior Office action, the teachings of the art suggest that only "neoplastic nucleic acids" that are mutated early in the process of carcinogenesis

associated with a particular type of cancer would be detectable prior to the development of histological evidence of that cancer, and, absent actual evidence that a particular mutation or mutations in a particular nucleic acid occur sufficiently early in the development of cancer so as to be detectable prior to histological changes in lymph nodes and/or surgical margins, one skilled in the art would not expect to be able to accomplish such detection. Applicant's specification provides no evidence that mutated versions of any of the nucleic acids recited in the instant claims can actually be detected in histologically normal surgical margins or lymph nodes in patients with any type of cancer. Further, the examiner was unable to identify any prior art supporting enablement of the claimed invention, and no such prior art or other evidence has been cited or provided by Applicant in response to the instant rejection. While Applicant's response asserts that one of skill in the art would recognize p53 as representative of the list of genes recited in Applicant's claims (for which no data has been shown), it is again noted that Nees et al indicate that mutation of p53 is likely an early event in head and neck carcinogenesis, such that mutations occur sufficiently early that they are present before histological evidence of cancer is present (see page 4189, right column of Nees et al). While Applicant's arguments regarding p53 might be persuasive given, e.g., evidence or teachings in the art that p53 and the genes of the instant claims are expressed contemporaneously, or, e.g., at a similar early time point in different cancers, absent such evidence or teachings, one of skill in the art would in fact have no reason to assume or predict that any of the genes of the claims could be employed in the same

manner as p53. Accordingly, Applicant's arguments are not persuasive, and this rejection is therefore maintained.

Conclusion

4. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Diana B. Johannsen whose telephone number is 571/272-0744. The examiner can normally be reached on Monday-Friday, 7:30 am-4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached at 571/272-0745. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Diana B. Johannsen
Primary Examiner
November 1, 2004